Listeria monocytogenes and *Escherichia coli* septicemia and meningoencephalitis in a 7-day-old llama

Nicholas Frank, Laurent L. Couëtil, Kathy-Anne Clarke

Abstract — *Listeria monocytogenes* and *Escherichia coli* were isolated from blood collected on presentation and tissue samples taken postmortem. *Listeria monocytogenes* was isolated from cerebrospinal fluid collected antemortem. The importance of passive transfer of immunity, the subtlety of neurologic signs in early meningitis, and considering blood-CSF penetration in antimicrobial selection are discussed.

Résumé — Septicémie et méningoencéphalite à *Listeria monocytogenes* et *Escherichia coli* chez un lama âgé de 7 jours. *Listeria monocytogenes* et *Escherichia coli* ont été isolés à partir du sang recueilli à la présentation de l'animal et à partir d'échantillons de tissus prélevés après la mort. *Listeria monocytogenes* a été isolé du liquide cérébrospinal chez l'animal vivant. L'importance du transfert passif de l'immunité, la subtilité des signes neurologiques en début de méningite et des considérations sur le passage de certains antimicrobiens du sang au liquide cérébrospinal y sont discutés.

(Traduit par docteur André Blouin)

Can Vet J 1998; 39: 100–102

A 7-day-old, 10-kg, female llama (*Lama glama*) was admitted with the complaint of weakness. The owner reported that following birth, the cria was recumbent for 12 h. Once standing the cria would not nurse from the dam and required bottle-feeding (90 mL goat milk, every 3 h). A total of 60 mL of dam's colostrum and 30 mL goat's colostrum were given in the first 24 h. At 6 d of age, the cria was weak and by the 7th day recumbent and no longer nursing.

The cria presented in lateral recumbency, weak, and lethargic. Abnormal findings on physical examination included dehydration, injected mucous membranes, fever (39.5°C, normal 37.7°C to 39.2°C), and tachycardia (140 beats/min, normal 60 to 90 beats/min) (1). Increased lacrimation, blepharospasm, and increased corneal opacity of the left eye were also noted. Subsequently, uveitis and bullous keratopathy were diagnosed on the basis of ophthalmologic examinations.

Hematologic findings included neutropenia with neutrophil toxicity, hyperfibrinogenemia, hemoconcentration, and hypoproteinemia following rehydration (Table 1). Abnormal blood chemistry values included hyperglycemia (20.2 mmol/L, normal 5.2 to 9.4 mmol/L) and elevated blood urea nitrogen (14.6 mmol/L, normal 3.6 to 7.6 mmol/L) (2). Both parameters returned to normal within 12 h. Blood gas analysis was normal. Blood for aerobic and anaerobic microbial culture was submitted. *Listeria monocytogenes* and *Escherichia coli* were subsequently isolated and reported 5 d later. Serum immunoglobulin measurement was not performed in this case due to an oversight.

Department of Veterinary Clinical Sciences (Frank, Couëtil) and Pathobiology (Clarke), Purdue University, School of Veterinary Medicine, 1248 Lynn Hall, West Lafayette, Indiana 47907-1248 USA.

The presumptive diagnosis of failure of passive transfer of immunity and septicemia was made, based upon the history and clinical findings. Hyperimmunized llama plasma (Triple J Farms, Redmond, Washington, USA; 300 mL, IV) was administered and antibiotic therapy initiated. Potassium penicillin G (Marsam Pharmaceuticals, Cherry Hill, New Jersey, USA; 22 000 IU/kg BW, IV, q6h) and amikacin sulfate (Amiglyde-V, Fort Dodge, Iowa, USA; 10 mg/kg BW, IV, q12h) were administered. Replacement (500 mL) and maintenance IV fluids (Plasma-Lyte, Baxter Healthcare, Deerfield, Illinois, USA; 100 mL/kg BW, q24h) were also provided. Goat milk (1L/d, representing 10% BW) was given via an indwelling nasogastric tube and supplemental IV parenteral nutrition initiated 36 h after presentation. Approximately 25% of the daily energy requirement was supplemented, IV, consisting of 68% glucose (Dextrose 50% solution, Phoenix Scientific, St. Joseph, Missouri, USA), 14% amino acids (8.5% Travasol Injection, Baxter Healthcare), and 18% lipid (Intralipid 20%, Pharmacia, Clayton, North Carolina, USA). Lipid provided 20% of nonprotein calories. Parenteral nutrition contributed 3.4 g nitrogen/d, with a nonprotein calorie to nitrogen ratio of 150:1.

The patient showed initial improvement and was soon able to stand with assistance but would not nurse. The cria's condition remained stable for 2 d, but deteriorated on the 3rd day. Neurologic deficits in the form of weakness, depression, and occasional intention tremors of the head were observed. In addition, leukogram results indicated a marked inflammatory process with increased neutrophil toxicity (Table 1). Cerebrospinal fluid (CSF) was submitted for cytological examination and aerobic and anaerobic microbial culture. Cytological examination revealed an increased number of leukocytes, composed primarily of neutrophils in different stages of degeneration, with large numbers of intracellular bacteria

Table 1. Hematological and cerebrospinal fluid analysis results from a 7-day-old llama with *Listeria monocytogenes* and *Escherichia coli* septicemia and meningoencephalitis

Blood	At presentation	Day 3[a]	Reference range (2)
Segmented neutrophils (×106/L)	1100	4830	1128–14 556
Band neutrophils (×106/L)	70	5330	0–487
Metamyelocytes (×106/L)	0	130	0
Fibrinogen (g/L)	6.0	5.0	1.0–4.0
Hematocrit (L/L)	0.45	0.33	0.24–0.35
Total protein (g/L)	56	43	47–61
Cerebrospinal fluid		**Day 3[a]**	**Reference range (3)**
Leukocytes (×106/L)		3000	0–3
Erythrocytes (×106/L)		1700	0–1360
Total protein (g/L)		3.12	0.32–0.67

[a]Days after presentation

(Table 1). *Listeria monocytogenes* was subsequently cultured from the CSF.

A diagnosis of bacterial meningitis was made, based on the results of the CSF cytological examination. Antimicrobial therapy was revised and cefoxitin (Mefoxin, Merck, West Point, Pennsylvania, USA; 20 mg/kg BW, IV, q6h) substituted. Anti-inflammatory drugs administered include dimethyl sulfoxide (DOMOSO, Syntex Animal Health, West Des Moines, Iowa, USA; 1g/kg BW as a 10% solution, IV, q24h) and dexamethasone (Azium, Schering-Plough Animal Health, Kenilworth, New Jersey, USA; 0.1 mg/kg BW, IV, q6h).

In the following 24 h, rapid deterioration in the patient's neurologic status was seen. Seizures developed that were initially controlled but became refractory to administered diazepam (Diazepam Injection, Elkins-Sinn, Cherry Hill, New Jersey, USA). Euthanasia was recommended due to the poor prognosis.

A postmortem examination was performed. Findings included gross and histologic lesions consistent with meningoencephalomyelitis, suppurative myocarditis, nephritis, and hepatitis. The leptomeninges of the cerebrum, midbrain, and cerebellum were infiltrated by neutrophils, lymphocytes, and plasma cells. Inflammatory cells extended along blood vessels into the neuropil. Similar lesions were seen throughout the spinal cord. *Listeria monocytogenes* and *E. coli* were isolated from brain, lung, and joint fluid samples taken postmortem.

Listeria monocytogenes and *E. coli* septicemia and meningoencephalitis in a neonatal llama has not been reported. In this case, it is likely that the septicemia developed due to a failure of passive transfer of immunity. Using a guideline of a 6% BW colostrum requirement in the first 24 h, this cria received only 15% of the volume recommended (1). Further measurement of serum immunoglobulin levels by zinc sulfate turbidity or radial immunodiffusion was not performed but would be beneficial in future cases. In utero infection was also considered due to the patient's inability to stand after birth. This theory was not supported by a uterine fluid swab collected from the dam 16 d after parturition. However, uterine clearance of bacteria could have occurred within this time (4).

The exact source of *L. monocytogenes* in this case is difficult to ascertain. The environment and infected animals are known reservoirs. In the environment, *Listeria* spp. can survive and multiply for months in cool, damp organic matter at near-neutral pH (5). Potentially infected animals in contact with this patient included the dam, 2 other llamas, and a herd of 9 pygmy goats that shared the pasture. If the dam was infected, increased fecal shedding may have been induced by the stress of parturition (6). However, the dam had produced 2 other crias in the past, both healthy. The owners had not observed any evidence of neurologic disease or abortions within the llama or goat herds.

Bacterial meningitis was diagnosed in this patient on the 3rd day of hospitalization. In retrospect, a subtle indication of neurologic disease may have been the cria's inability to nurse, seen from the day of presentation. Fine intention tremors of the head, induced by handling, were also noticed occasionally, but attributed to fear. In future, such signs should prompt further diagnostic investigation to rule out bacterial meningitis.

Antimicrobial selection is important in cases of bacterial septicemia and meningitis. Sensitivity of the isolates to the antimicrobial and blood-CSF barrier penetration are key factors. In addition, when treating *L. monocytogenes* infection, the intracellular location of the bacteria further reduces antimicrobial effectiveness. Three antimicrobial drugs were used in this patient. Penicillin and amikacin were combined, and cefoxitin was substituted later. All *L. monocytogenes* isolates from this cria were sensitive to penicillin and amikacin. Cefoxitin was not included in the profile, therefore the sensitivity of the *L. monocytogenes* isolates to this 2nd generation cephalosporin remains unknown. For the 2 cephalosporins included, sensitivity was recorded to cephalothin (1st generation), but not ceftiofur sodium. *Escherichia coli* isolates were sensitive to amikacin and both cephalosporins.

From research in human beings, it is recognized that CSF antimicrobial concentrations should exceed 10 to 30 times the minimum bactericidal concentration to be effective in cases of bacterial meningitis (7). Attaining these levels is dependent upon the physicochemical properties of the drug and its ability to penetrate the lipid bilayer of the blood-CSF barrier. Early in bacterial meningitis, lipid-soluble, low molecular weight drugs are ideal. Later in the disease, inflammation increases barrier permeability.

The 3 antimicrobials selected in this case were not ideal early in the disease. Penicillins are non-lipid-soluble, weak organic acids, and amikacin has a high

molecular weight and is polar. Second generation cephalosporins do not penetrate the intact blood-CSF barrier well (7). In future cases, another antimicrobial, such as cefotaxime sodium, a 3rd generation cephalosporin, may be selected. Cefotaxime has been used successfully in the treatment of bacterial meningitis in foals and crosses membranes well (8). However, interestingly, *L. monocytogenes* isolates from this patient were resistant to ceftiofur sodium.

The anti-inflammatories administered to this patient included dexamethasone. The use of corticosteroids in the treatment of bacterial meningitis is controversial. Dexamethasone has been advocated for use in human neonates with bacterial meningitis, when it is administered 15 to 20 min before antibiotics and maintained until clinical signs resolve (9). Corticosteroids are reported to reduce indices of meningeal inflammation, including CSF pressure and cytokine concentrations (9). In this cria, rapid deterioration in neurologic status was seen within 24 h of initiating dexamethasone therapy. However, by only administering corticosteroid in the late stages of the disease, it is difficult to draw conclusions about the merit of this therapy.

Isolation of *L. monocytogenes* from the cria raised the issue of human exposure to a zoonotic disease. The disease and its zoonotic potential were discussed with the owners. They were asked to consult their physician and inform him or her of their exposure to the cria, if any symptoms of illness developed in the following weeks.

Meningitis remains a frustrating disease to detect and treat. Patients early in the course of the disease are difficult to assess. The clinician should always rule out bacterial meningitis when presented with a depressed neonatal llama. In addition, careful attention should be paid to the physicochemical properties of the antimicrobials selected and their attainable CSF concentrations.

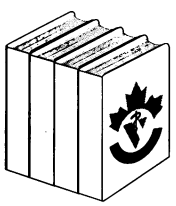
Acknowledgment

The authors thank former student Dr. James Weisman for his excellent patient care. CVJ

References

1. Fowler ME. Medicine and Surgery of South American Camelids. Ames: Iowa State Univ Pr, 1989: 327–336.
2. Fowler ME, Zinkl JG. Reference ranges for hematologic and serum biochemical values in llamas (*Lama glama*). Am J Vet Res 1989; 50: 2049–2053.
3. Welles EG, Pugh DG, Wenzel JGW, Sorjonen DC. Composition of cerebrospinal fluid in healthy adult llamas. Am J Vet Res 1994; 55: 1075–1079.
4. Osebold JW, Kendrick JW, Njoku-Obi A. Abortion of cattle experimentally with *Listeria monocytogenes*. J Am Vet Med Assoc 1960; 137: 227–233.
5. Dennis SM. Listeriosis (circling disease, silage sickness). In: Howard JL, ed. Current Veterinary Therapy 3. Food Animal Practice. Philadelphia: WB Saunders, 1993: 580–583.
6. Wesley IV, Bryner JH, Van Der Maaten MJ, Kehrli M. Effects of dexamethasone on shedding of *Listeria monocytogenes* in dairy cattle. Am J Vet Res 1989; 50: 2009–2013.
7. Jamison JM, Prescott JF. Bacterial meningitis in large animals. Part II. Compend Contin Educ Pract Vet 1988; 10: 225–232.
8. Morris DD, Rutkowski J, Lloyd KC. Therapy in two cases of neonatal foal septicaemia and meningitis with cefotaxime sodium. Equine Vet J 1987; 19: 151–154.
9. Odio CM, Faingezicht I, Paris M, *et al.* The beneficial effects of early dexamethasone administration in infants and children with bacterial meningitis. N Engl J Med 1991; 324: 1525–1531.

Books Received



Livres reçus

Through the generosity of several book publishers, the ***Canadian Veterinary Journal*** *is able to inform readers of new publications that are now available to veterinary practitioners. Readers are invited to contact their local library, the publishers listed here, or the bookstores of Canadian veterinary colleges should they wish to obtain their own copies.*

Grâce à la générosité d'un grand nombre d'éditeurs, la **Revue vétérinaire canadienne** est en mesure de tenir ses lecteurs au courant des nouvelles publications rendues disponibles aux médecins vétérinaires. On encourage les lecteurs qui désirent obtenir une de ces publications à entrer en contact avec leur bibliothèque, avec les éditeurs listés ci-bas ou avec les librairies aux facultés de médecine vétérinaire.

- Bojrab MJ, Ellison GW, Slocum B. ***Current Techniques in Small Animal Surgery, 4th ed.*** Williams and Wilkins, Media, Pennsylvania, 1997. 1340 pp. ISBN 0683-00890-0. $99.95 US
- Crow SE, Walshaw SO. ***Manual of Clinical Procedures in the Dog, Cat & Rabbit, 2nd ed.*** Lippincott-Raven Publishers, Hagerstown, Maryland, 1997. 322 pp. ISBN 0-397-51588-X. $34.95 US
- Fields-Babineau M. ***Dog Training Basics.*** Sterling Publishing Company, New York, 1997. 128 pp. ISBN 0-8069-9406-1. $19.95 US
- Grandin T. ***Genetics and the Behavior of Domestic Animals.*** Academic Press, San Diego, 1998. 355 pp. ISBN 0-12-295130-1. $69.95 US
- Mair T, Love S, Schumacher J, Watson E. ***Equine Medicine, Surgery and Reproduction.*** W.B. Saunders, Philadelphia, 1997. 498 pp. ISBN 0-7020-1725-6. $117.00 US
- Morgan RV. ***Handbook of Small Animal Practice, 3rd ed.*** W.B. Saunders, Philadelphia, 1997. 1436 pp. ISBN 0-7216-3329-3. $218.00 US
- Reedy LM, Miller WH Jr, Willemse T. ***Allergic Skin Diseases of Dogs and Cats, 2nd ed.*** W.B. Saunders, Philadelphia, 1997. 267 pp. ISBN 0-7020-1974-7. $67.95 US
- Youngquist RS. ***Current Therapy in Large Animal Theriogenology.*** W.B. Saunders, Philadelphia, 1997. 898 pp. ISBN 0-7216-5396-0. $189.00 US